Remarks

Reconsideration of this Application is respectfully requested. Entry of this amendment after final rejection is respectfully requested to put the claims in condition for allowance.

Upon entry of the foregoing amendment, claims 12, 13, 17-20, 24-32 and 34-38 are pending in the application, with claims 12, 34 and 36 being the independent claims. Support for the amendments to claims 12, 34, 36 and 38 appears, *inter alia*, in the specification as-filed on page 41, lines 6-10. These changes are believed to introduce no new matter, and their entry is respectfully requested.

Based the above amendments and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

I. Interview

Applicants wish to thank the Examiner for the telephone interview of July 19, 2005, during which the issue of written descriptive support under 35 U.S.C. §112(1) was discussed. Applicants requested that Examiner Marschel reconsider the rejections of the July 13, 2005 Office Action in light of the March 2, 2005 Amendment and Reply and the October 6, 2004 in-person interview. Examiner Marschel agreed to reconsider the July 13, 2005 rejections.

II. Rejections under 35 U.S.C. §112(1)

A. Claims 12, 13, 17-20, 24-32 and 34-38

Claims 12, 13, 17-20, 24-32 and 34-38 have been rejected under 35 U.S.C. § 112(1), as failing to comply with the written description requirement. Applicants respectfully traverse this rejection. (*See* July 13, 2005 Office Action).

An objective standard for determining compliance with the written description requirement of 35 U.S.C. §112, first paragraph, is, "does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed." *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989), *see also* MPEP 2163.02 (2004). An applicant may show possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997). Possession may be shown by (1) a description of actual reduction to practice, or (2) by showing that the invention was "ready for patenting" such as by the disclosure of drawings or structural chemical formulas that show that the invention was complete, or (3) by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention. *See,* e.g., *Pfaff v. Wells Elecs., Inc.*, 525 U.S. 55, 68, 119 S.Ct. 304, 312, 48 USPQ2d 1641, 1647 (1998); *Regents of the University of California v. Eli Lilly*, 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997); *Amgen v. Chugai Pharmaceutical*, 927 F.2d 1200, 1206, 18 USPQ2d 1016, 1021 (Fed. Cir. 2001); *see also* MPEP 2163.02 (2004). Furthermore, the Applicant is not required to describe *exactly* the subject matter claimed, but instead the description must allow persons of ordinary skill in the art to recognize that he or she invented what is claimed. *See Union Oil Co. of California v. Atlantic Richfield Co.*, 208 F.3d 989, 997 (Fed. Cir. 2000), citing *In re Goseli*, 872 F.2d 1008, 1012 (Fed. Cir. 1989).

The "Methodology for Determining Adequacy of Written Description" found at section 2163.II.A.2. of the MPEP provides that, prior to determining whether the disclosure satisfies the written description requirement for the claimed subject matter, an

Examiner should review the claims and the *entire specification, including the specific embodiments, figures, and sequence listings*, to understand how the Applicant provides support for the various features of the claimed invention. In this case, the Examiner has not considered the entire specification, including the specific embodiments and figures, prior to determining whether the disclosure provides adequate support for a supplemented tissue sealant wherein the amount of said supplement is greater than the amount which is soluble in said fibrin matrix. In the Amendment and Reply of March 2, 2005, and the in-person interview of October 6, 2004, Applicants pointed to text, examples and figures throughout the disclosure which demonstrate that the inventors had possession of the presently-claimed invention at the time of filing. The Examiner's remarks in the July 13, 2005 Office Action indicate that rather than reviewing the entire disclosure to understand the invention as a whole and to put the highlighted sections of the specification into context, the Examiner extracted portions of the submitted excerpts when considering the written description requirement.

For example, the Examiner has asserted that the phrase "said effective amount of said supplement is greater than the amount which is soluble in said fibrin matrix" is not fully supported by the specification.(*See* July 13, 2005 OA, page 2). Specifically, he argues that generic supplementation of the tissue sealant is not supported, and he states that the portions of the specification pointed to by Applicants are limited to particular compounds:

> Applicants point to page 22, lines 4-16, for support. Consideration of said page 22 citation reveals that only the inclusion of compounds such as free TET etc. confers extended longevity which can be exploited to increase duration of a drug's release. This fails to provide written basis for any solubility or insolubility practice whatsoever, nor such solubility or insolubility in a fibrin matrix.

(July 13, 2005 OA, pages 2-3).

Contrary to the Examiner's assertions, the specification at page 22, lines 4-16 provides written description for sustained release of poorly soluble drugs from a fibrin matrix generally, but also mentions certain antibiotics as examples of supplements:

> The studies reported herein unexpectedly demonstrate that the inclusion of compounds such as the free base TET or ciprofloxacin (CIP) HCl, in FG or the treatment of FG therewith confers extended longevity to the supplemented FG. This phenomenon can be exploited to increase the duration of a drug's release from the TS...In general, poorly water soluble forms of a drug, such as the free base of TET, increase the delivery of the drug from the TS more than freely water soluble forms thereof.

Additionally, the specification at page 21 provides a long list of drugs that can be used on the present invention, which further contradicts the Examiner's statement that the specification recites only specific drugs such as TET, and does not provide support for the generic term "supplement" recited in claims 12, 32 and 34. A person of ordinary skill in the art would recognize from reviewing pages 21 and 22 in light of the entire specification, that sustained release of drugs from a fibrin matrix when present above their solubility limits is a phenomenon that applies generically to many supplements. (*see* Declaration of Julia Lathrop ("Lathrop Declaration," p. 3). There is nothing in the application that states or suggests that sustained release of a supplement from a fibrin matrix when the supplement is present in the fibrin matrix above its solubility limit is limited to TET. Thus, the disclosure of pages 21 and 22, considered in light of the application as a whole, provides support for sustained release of a supplement from fibrin matrix, wherein the effective amount of the supplement is greater than the amount which is soluble in the fibrin matrix.

The Examiner has also asserted that the specification at page 104, lines 27-29 does not provide adequate written basis for the requirement that the effective amount of

the supplement is greater than the amount which is soluble in the fibrin matrix. (*See* July 13, 2005 OA, page 3). Applicants respectfully disagree.

As previously discussed during the in-person interview of October 6, 2004, and in the Amendment and Reply filed on March 2, 2005, the specification at pages 104, 107-109, and Figures 23, 24, 25, 28, 31 and 32, considered in light of the application as a whole, provide adequate written descriptive support for the phrase "said effective amount of said supplement is greater than the amount which is soluble in said fibrin matrix." (*see* March 2, 2005, Amendment and Reply, pages 18 and 19). A person of ordinary skill in the art of fibrin sealant formulation and use, upon review of the application, including the examples and figures, would recognize that the sustained release of a supplement from a fibrin matrix may be achieved when the amount of supplement is greater than that which is soluble in the fibrin matrix, as recited in claims 12, 34 and 36. (*see* Lathrop Declaration, pp. 3-4).

A person of ordinary skill in the art would also know how to determine the solubility limit of a supplement in a solvent:

> one way to determine the solubility limit of a particular medium, such as fibrin sealant, is to add the supplement to the medium until that supplement no longer remains in solution or dissolves in the medium, but instead precipitates out of solution.

(Lathrop Declaration, p. 5). Thus, a person of ordinary skill in the art would understand from the above-cited text and figures that one would merely need to add an amount of supplement that is greater than the amount needed to reach the solubility limit in a fibrin matrix to practice the disputed element of the invention of claims 12, 34 and 36 (and those claims depending therefrom). Accordingly, Applicants respectfully assert that

claims 12, 34 and 36 are in compliance with the written description requirement of 35 U.S.C. §112; therefore it is respectfully requested that this rejection be withdrawn.

B. Claims 12, 34 and 36

The Examiner has rejected independent claims 12, 34 and 36 under 35 U.S.C. §112, first paragraph, asserting that the phrase "substantially free of protease inhibitors" contains new matter. Solely to advance prosecution, and not in acquiescence of any of the Examiner's assertions, Applicants have amended claims 12, 34 and 36 to recite "substantially free of added protease inhibitors," as suggested by Examiner Marschel. Support for this amendment may be found, *inter alia*, at page 41, lines 6-10 of the application as-filed. Reconsideration and withdrawal of this rejection is requested.

III. Rejections under 35 U.S.C. §103

The Examiner has maintained the rejection in the previous Office Action of claims 17, 18, 25, 29-32 and 35-38 under 35 U.S.C. §103(a) as obvious over Marx [P/N 5,607,694] ("Marx"), taken in view of Popescu *et al.* [P/N 4,708,861] ("Popescu"). At page 9 of the Office Action dated July 2, 2004, the Examiner noted that based on the earlier discussed new matter rejections, he is only considering the effective filing date of June 7, 1995, and has not accorded the present application the proper priority date of March 12, 1993, as stated in the specification.[1]

As discussed in the interview of October 6, 2004, the Amendment and Reply of March 2, 2005, and as discussed above, Applicants respectfully assert that the new matter rejection under §112 has been overcome; thus the priority date of March 12, 1993

[1] USSN 08/479,038 is a continuation-in-part of USSN 08/351,006, filed December 7, 1994, which is a continuation-in-part of USSN 08/328,552, filed October 24, 1994, which is a continuation-in-part USSN 08/031,164, filed March 12, 1993, abandoned, which is a continuation-in-part of USSN 07/618,419 and 07/798,919, filed November 27, 1990, and November 27, 1991, respectively, both of which are abandoned.

for the claims at issue is proper. Accordingly, Marx is not available as prior art under 35 U.S.C. §102, because its earliest claim to priority occurred after this date.

Solely to advance prosecution and not in acquiescence of any of the Examiner's assertions, Applicants have requested that claims 12, 34, 36 and 38 be amended to exclude liposomes. Both Marx and Popescu disclose compositions that require liposomes, therefore they do not meet all the elements of the presently pending claims. Further, neither Marx nor Popsecu, alone or in combination, suggests a supplement delivery system for sustained release of the supplement from a fibrin matrix which is substantially free of liposomes. Thus, Applicants assert that none of the presently pending claims are obvious over Marx and Popsecu, alone or in combination. Accordingly, withdrawal of this rejection is respectfully requested.

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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